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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/780,484	02/17/2004	David B. Rozema	Mirus.030.16.04	2135

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EXAMINER
EPPS -SMITH, JANET L

ART UNIT	PAPER NUMBER
1633	

MAIL DATE	DELIVERY MODE
07/21/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/780,484	ROZEMA ET AL.	
	Examiner	Art Unit	
	Janet L. Epps-Smith	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 April 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-7 and 10-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-7 and 10-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1-26-09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office Action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed 4-22-09 has been entered.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

3. Clams 1, 3-7, and 10-20 are presently pending.

Response to Arguments

Claim Rejections - 35 USC § 102

4. The rejection of claims 1, 3-5, 7, 10-15, 17, and 19-20 under 35 U.S.C. 102(b) as being anticipated by Wolff are withdrawn in response to Applicant's arguments.

Claim Rejections - 35 USC § 103

5. Applicant's arguments with respect to claims 1, 3-7, and 10-20 have been considered but are moot in view of the new ground(s) of rejection.

6. Claims 1, 3-7, and 10-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wolff (WO200075164 A1), in view of Mathiowitz et al. (US 6248720) and Haines et al. (US6479464).

7. WO 200075164 teach the following at page 7:

Polymers for Drug and Nucleic Acid Delivery

Polymers are used for drug delivery for a variety of therapeutic purposes. Polymers have also been used in research for the delivery of nucleic acids (polynucleotides and oligonucleotides) to cells with an eventual goal of providing therapeutic processes. Such processes have been termed gene therapy or anti-sense therapy. One of the several methods of nucleic acid delivery to the cells is the use of DNA-polycation complexes. It has been shown that cationic proteins like histones and protamines or synthetic polymers like polylysine, polyarginine, polyornithine, DEAE dextran, polybrene, and polyethylenimine may be effective intracellular delivery agents while small polycations like spermine are ineffective. The following are some important principles involving the mechanism by which polycations facilitate uptake of DNA:

Polycations provide attachment of DNA to the cell surface. The polymer forms a cross-bridge between the polyanionic nucleic acids and the polyanionic surfaces of the cells. As a result the main mechanism of DNA translocation to the intracellular space might be non-specific adsorptive endocytosis which may be more effective then liquid endocytosis or receptor-mediated endocytosis. Furthermore, polycations are a convenient linker for attaching specific ligands to DNA and as result, DNA- polycation complexes can be targeted to specific cell types.

At page 23 of this reference, compound delivery systems comprising polymers containing pH-labile groups are described as follows:

In some preferred embodiments of the present invention, nucleic acids are delivered to cells by a polymer complex containing a labile group, or groups, that undergoes chemical transformation when exposed to the low pH environment of an endosome. Such complexes provide improved nucleic acid delivery systems, as they provide for efficient delivery and low toxicity.

At page 25 of this reference biologically active compounds containing pH-labile bonds, Described in the following paragraphs on page 26 of the reference:

> The invention specifies compounds of the following general structure: A-B-C wherein A is a biologically active compound such as pharmaceuticals, drugs, proteins, peptides, hormones, cytokines, enzymes and nucleic acids such as anti-sense, ribozyme, recombining nucleic acids, and expressed genes; B is a labile linkage that contains a pH-labile bond such as acetals, ketals, enol ethers, enol esters, amides of 2,3-disubstituted maleamic acids, imines, imminiums, enamines, silyl ethers, and silyl enol ethers; and C is a compound. In one embodiment C is a compound that modifies the activity, function, delivery, transport, shelf-life, pharmacokinetics, blood circulation time in vivo, tissue and organ targetting, and sub-cellular targeting of the biologically active compound A. For example, C can be a hydrophilic compound such as polyethylene glycol to increase the water solubility of relatively hydrophobic drugs (*e.g.* amphotericin B) to improve their formulation and delivery properties. In other embodiments, B is a labile linkage that contains pH-labile bond such as acetals, ketals, enol ethers, enol esters, amides, imines, imminiums, enamines, silyl ethers, and silyl enol ethers.

Page 32 of this reference describes transfection reagents that mediate entry of oligonucleotides/polynucleotides into cells, this reference includes polyamines, and peptides such as membrane active compounds such as melittin described on page 38.

The polymers of this reference also includes amphipathic polymers within the context of their delivery compounds, see page 37.

Pages 51-52 of this reference describes the modification of amine functions in the polymers of the present invention with compounds such as can anhydride (such as maleic and succinic anhydride) to form an amide acid, this reference teaches that the product of succinic anhydride and a primary amine, reverses back to an amide and anhydride, this reaction is pH sensitive. Wolf et al. also teach that linker or spacer molecules can be used to conjugate passenger or carrier molecules to the amine

groups of the polymers of their invention. These molecules increase the transport and delivery of passenger molecules (page 52, lines 1-4).

8. It would have been obvious to the ordinary skilled artisan at the time of the instant invention, to modify the nucleic acid delivery compounds of Wolff et al. to comprise a polyamine-polynucleotide conjugate linked via a labile covalent bond since this is clearly described at page 26 of Wolff et al. Furthermore, it would have been obvious to further modify this conjugate to comprise wherein the polyamide polymer further comprises conjugate passenger or carrier molecules linked by labile bond since these molecules are disclosed by Wolff et al. to increase the transport and delivery of the complex into cells, see page 52 of Wolff et al.

9. However, Wolff does not teach the use of polyvinyl ether in their transfection complexes. Mathiowitz et al. teach that polyvinylethers are functionally equivalent polymers useful for the transfection of nucleic acid into cells.

10. Wolff does not teach the use of paradaxin in their transfection complexes. Haines et al. teaches the use of the fusogenic amphipathic peptide sequence paradaxin as a ligand with serves to promote cellular uptake of nucleic acid by disrupting cellular membranes.

11. It would have been obvious to the ordinary skilled artisan to modify the polymer portion of the transfection compounds of Wolff with the polymers of Mathiowitz et al. and Haines et al. since these references teach the usefulness of polymers such as polyvinylether (Mathiowitz et al.) and paradaxin (Haines et al.) in the transfection of nucleic acids into cells. Therefore, it would have been obvious to substitute art

recognized nucleic acid transfection polymers for the polymers described in Wolff since the prior art polymers are disclosed as functionally equivalent to those polymers described in Wolff.

12. See MPEP § 2144.06 [R-6].II., which describes the obviousness of "[S]UBSTITUTING EQUIVALENTS KNOWN FOR THE SAME PURPOSE:

13. In order to rely on equivalence as a rationale supporting an obviousness rejection, the equivalency must be recognized in the prior art, and cannot be based on applicant's disclosure or the mere fact that the components at issue are functional or mechanical equivalents. In re Ruff, 256 F.2d 590, 118 USPQ 340 (CCPA 1958) (The mere fact that components are claimed as members of a Markush group cannot be relied upon to establish the equivalency of these components. However, an applicant's expressed recognition of an art-recognized or obvious equivalent may be used to refute an argument that such equivalency does not exist.); ** Smith v. Hayashi, 209 USPQ 754 (Bd. of Pat. Inter. 1980) (The mere fact that phthalocyanine and selenium function as equivalent photoconductors in the claimed environment was not sufficient to establish that one would have been obvious over the other. However, there was evidence that both phthalocyanine and selenium were known photoconductors in the art of electrophotography. "This, in our view, presents strong evidence of obviousness in substituting one for the other in an electrophotographic environment as a photoconductor." 209 USPQ at 759.)."

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Epps-Smith whose telephone number is 571-272-0757. The examiner can normally be reached on M-F, 10:00 AM through 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Janet L. Epps-Smith/
Primary Examiner, Art Unit 1633